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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
08/958,570	10/28/97	GREGORY	R 16930-000921

EXAMINER

HM11/0720

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ART UNIT	PAPER NUMBER
1636	4

DATE MAILED: 07/20/98

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 10/28/97

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire Three (3) month(s), ~~or thirty days,~~ whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 16-24 and 26-31 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☑ Claim(s) 16-24 and 26-31 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☑ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☑ Notice of Reference Cited, PTO-892

☑ Information Disclosure Statement(s), PTO-1449, Paper No(s). 2

☐ Interview Summary, PTO-413

☑ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

– SEE OFFICE ACTION ON THE FOLLOWING PAGES –

* U.S. GPO: 1996-410-238

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 16-24 and 26-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants claim methods of treating pathologies (i.e. cancers) via gene therapy protocols using claimed adenoviral vectors comprising a partial or total deletion of the protein IX gene and a gene encoding a functional anti-tumor gene (i.e. a tumor suppressor gene or suicide gene or suicide gene, such as HSV TK, and a thymidine kinase metabolite.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation (*United States v. Teletronics Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988). Whether undue experimentation is needed is not based upon a single factor but rather is a conclusion reached by weighing many factors (See *Ex parte Forman*, 230 USPQ 546 Bd. App. & Inter. 1986 and *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). These factors include the following;

1) Unpredictability of the art. The gene therapy art at the time the invention was made was extremely unpredictable. This unpredictability is manifested at the levels of vector design for *in*

vivo delivery of transgenes to target cells, the level of efficiently delivering the transgenes to target cells, the transient and unpredictable expression of transgenes in target cells, etc. (See Orkin et al., "Report to the NIH Panel", see whole document, particularly pp. 6-11; and Verma et al., Nature, Vol. 389, 9/18/97, pp. 239-242, see whole article, particularly pp. 239 and 241 for reviews). With regard to use of gene therapy protocols involving tumor suppressor genes and "pro-drug" based strategies for treatment of cancer, Ross et al. (Human Gene Therapy, Vol. 7, 1996, pp. 1781-1790, see whole article, particularly pp. 1783 and 1786) notes that these therapies are (years after applicants' invention) still totally experimental with little or no evidence of efficacy in patients. The reasons for failure of these therapies *in vivo* is not explained.

2) State of the art. The gene therapy art at the time of applicants' invention was poorly developed. As noted by Orkin et al. in 1995 and by Verma et al. in 1997, no gene therapy protocol had been unambiguously proven to be successful *in vivo*. With regard to use of adenoviral vectors for treatment of cancer, it is noted that Verma et al., as late as Sept. 1997, notes that use of adenoviral vectors to treat cancer is ***still only a "promising approach"*** which still apparently has not been reduced to practice in patients.

3) Number of working examples. Applicants present no working examples of the claimed invention.

4) Amount of guidance presented by applicants. Applicants present some *in vitro* data and *in vivo* data using nude mice bearing Hep3B tumors. However, it is unclear how these data relate to the treatment of cancers in patients and if this *in vitro* and mouse data is art recognized as being

reasonably predictive of results which would be expected in patients. Applicants' in the instant specification do not provide teachings whereby the skilled artisan would overcome the art recognized problems associated with successful practicing of gene therapy in patients and indeed, do not even address these critical issues.

5) Scope of the claims. The claims read broadly on treatment of any of thousands of different pathologies in animals or humans or potentially hundreds of different cancers in animals or humans. The scope of the claims must be considered to be extremely broad.

6) Nature of the invention. The invention involves one of the most complex, unpredictable areas of molecular biology and medicine, the use of gene therapy procedures to treat pathologies in humans or animals.

7) Level of skill in the art. The level of skill in the gene therapy art is very high; however, those of preeminent skill in the art were unable to reduce to practice successful gene therapy years after the priority date of applicants' invention.

The kit recited in claim 31 is included in this rejection because a kit for practicing a non-enabled invention is likewise not enabled.

Given the above analysis of the factors which the courts have indicated are critical in determining whether a given invention is enabled, it must be considered that the skilled artisan would have had to have practiced undue and excessive experimentation in order to practice the claimed invention.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 23 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The members of the group of tumors listed in claim 23 should be separated by -- or-- rather than "and" since the claim as written reads on a tumor cell which is all of the recited tumors rather than one type of tumor selected from the list.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo whose telephone number is (703) 308-1906. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, George Elliott, can be reached on (703) 308-4003. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242 or (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

David Guzo
July 17, 1998

DAVID GUZO
PRIMARY EXAMINER